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(30) Priority data:
07/830,304 31 January 1992 (31.01.92) US

(71) Applicant: GENSIA, INC. [US/US]; 11025 Roselle Street, San Diego, CA 92121 (US).

(72) Inventors: VALCKE, Christian, Paul ; 10667 Wilkins Avenue #2, Los Angeles, CA 90024 (US). BOCHENKO, Walter, John ; 2258 9th Street, Encinitas, CA 92024 (US). HILLMAN, Robert, Steven ; 13134 Janetta Place, San Diego, CA 92130 (US).

(74) Agents: MURPHY, David, B. et al.; Lyon & Lyon, 611 West 6th Street, 34th Floor, Los Angeles, CA 90017 (US).

(81) Designated States: CA, FI, JP, NO, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

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(54) Title: METHOD AND APPARATUS FOR CLOSED LOOP DRUG DELIVERY

(57) Abstract

A closed-loop drug delivery system uses patient response and rule based decision making methods to achieve operator specified responses for diagnostic purposes. In the preferred embodiment, cardiac diagnosis is performed by pharmacologically stressing the heart by administration of an exercise simulating agent drug. In the preferred method, a protocol is defined, which preferably includes a target for a physiologic variable, such as heart rate, and a plan to achieve that target value. Preferably, the plan includes a specification of the desired rate of increase in that variable, such as the rate of increase in the heart rate per minute. The plan comprises the desired changes in the physiologic variable as a function of time. While any desired function may be used, the more common modes include RAMP, HOLD, LEVEL and TARGET mode. In one aspect of this invention, the protocol may be varied by the operator after drug administration has begun. Futher, in one embodiment, the protocol includes a definition of an acceptable zone of deviation from the plan, such that if the patient physiologic variable deviates from the permissible zone, alternate control rules are implemented. Preferably, saturation detection and avoidance is implemented.

CORRECTED VERSION*

PCT

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A3

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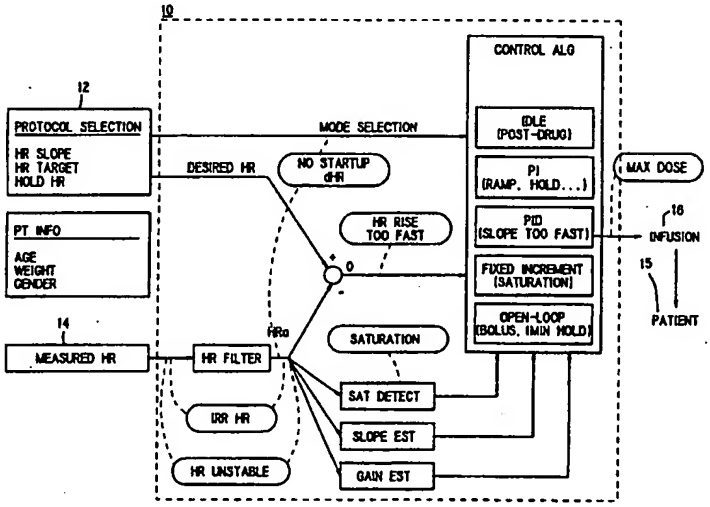

(57) Abstract

A closed loop drug delivery system uses patient response and rule based decision making methods to achieve operator specified responses for diagnostic purposes. Cardiac diagnosis is performed by pharmacologically stressing the heart by administration of an exercise simulating drug. A protocol is defined, which includes a target for a physiologic variable, such as heart rate, and a plan to achieve that target value. The plan includes a specification of the desired rate of increase in that variable, such as the rate of increase in the heart rate per minute. The plan comprises the desired changes in the physiologic variable as a function of time. While any desired function may be used, the more common modes include RAMP, HOLD, LEVEL and TARGET mode. The protocol may be varied by the operator after drug administration has begun. Further, the protocol includes a definition of an acceptable zone of deviation from the plan.

* (Referred to in PCT Gazette No. 03/1994, Section II)

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GA	Gabon				

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/00676

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61M 31/00
US CL :604/66

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/65-67; 128/Dig.12, Dig.13

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS: Exercise (W) Stimulating (W) agent?

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---, P Y	US, A, 5,108,363 (Tuttle et al.) 28 April 1992. See entire document.	1-9, 12, 13, 16-37, 39-50, 52-66 and 68-70 --- 10, 11, 14, 15, 38, 51, 67
Y	US, A, 4,871,351 (Feingold) 03 October 1989. See column 2, line 33 - column 3, line 23.	1-70
A	US, A, 4,718,891 (Lipps) 12 January 1988. See Abstract.	1-70

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
19 May 1993

Date of mailing of the international search report
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/00676

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A, 4,551,133 (Zegers de Beyl et al.) 05 November 1985. See Abstract.	1-70
A	US, A, 4,533,346 (Cosgrove, Jr. et al.) 06 August 1985. See Abstract.	1-70
A	US, A, 4,392,849 (Petre et al.) 12 July 1983. See Abstract.	1-70